

Gene Section

Short Communication

NT5E (5'-nucleotidase, ecto (CD73))

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Identity

Other names: CD73, E5NT, NT, NT5, NTE, eN, eNT

HGNC (Hugo): NT5E

Location: 6q14.3

DNA/RNA

Transcription

Two transcript variants encoding different isoforms have been found for this gene.

Variant 1 represents the longer transcript and encodes the longer isoform 1, 9 exons, transcript length 3548 bps, translation length 574 residues; variant 2 lacks an alternate in-frame exon compared to variant 1, 8 exons, transcript length 3384 bps, translation length 524 residues.

Protein

Description

There are two isoforms of NT5E. 5'-nucleotidase isoform 1 preproprotein, 574 amino acids; 5'-nucleotidase isoform 2 preproprotein, 524 amino acids. Isoform 2 has the same N- and C-termini but is shorter compared to isoform 1.

The NT5E preproprotein is further processed into a mature form, which consists of a dimer of 2 identical 70-kD subunits bound by a glycosyl phosphatidyl inositol linkage at its C-terminus to the external face of the plasma membrane.

Expression

CD73 is a cell surface enzyme found in most

tissues and many cell types including subsets of lymphocytes, macrophages, dendritic cells, endothelial cells and epithelial cells.

Hypoxia induces CD73 mRNA, protein expression and increases CD73 activity in mouse microvascular endothelial cells.

Particularly, CD73 is highly expressed in many human solid tumors, and its elevated expression and activity are associated with tumor invasiveness and metastasis and with shorter patient survival.

The RNA expression and enzyme activity of CD73 are variable in different breast cancer cell lines. For more details see gene expression pattern of NT5E.

Localisation

Plasma membrane.

Function

CD73 is an ectoenzyme (ecto-50-nucleotidase, EC 3.1.3.5).

It catalyzes conversion of AMP to adenosine. Adenosine exerts its effects via adenosine receptor A1, adenosine receptor A2A, adenosine receptor A2B and adenosine receptor A3.

CD73 has many physiological roles, such as regulation of barrier function, adaptation to hypoxia, ischemic preconditioning, anti-inflammation, leukocyte extravasation.

Expression and activity of CD73 on cancer cells is associated with poor prognosis and may promote metastasis.

CD73 facilitates the adhesion, migration, invasion of human breast cancer cells and proliferation of glioma cells and these processes are dependent upon the enzyme's production of adenosine.



The NT5E gene is located on the long (q) arm of chromosome 6 between positions 14 and 21. More precisely, the NT5E gene is located from base pair 86159301 to base pair 86205508 on chromosome 6.

Implicated in

Melanoma

Note

Deregulation of NT5E expression in melanoma occurs via epigenetic changes in the NT5E CpG island. Confirmation of the results in larger clinical series would support the candidacy of NT5E as a clinical biomarker in melanoma, which could be applied in both primary and relapsed disease. Inhibition of NT5E may have therapeutic potential in melanoma, particularly in patients with more aggressive disease metastasis to viscera or the brain.

Colorectal cancer

Note

CD73 expression in colorectal cancer is significantly higher than in normal colorectal tissues.

Prognosis

Patients with high expression of CD73 had a poorer overall survival rate compared with patients with low expression of CD73 in both cohorts. High expression of CD73 can be an independent and useful biomarker for predicting the poor survival of patients with colorectal cancer.

Chronic lymphocytic leukemia

Note

CD73-generated extracellular adenosine in chronic lymphocytic leukemia increases cytoplasmic cAMP levels by activation of the ADO receptors, inhibiting chemotaxis and limiting spontaneous drug-induced apoptosis of chronic lymphocytic leukemia cells.

Glioma

Note

Adenosine induced an increase in glioma cell adhesion. Ecto-5'-NT/CD73, an important producer of extracellular adenosine, may modulate glioma cell adhesion and tumor cell-extracellular matrix interactions.

Breast cancer

Note

CD73 plays an important role in breast cancer growth by affecting cell cycle progression and apoptosis. CD73 overexpression increased cell viability and promoted cell cycle progression, depending on its enzyme activity.

CD73 may facilitate the adhesion, migration and invasion of human breast cancer cells through its enzyme activity of generating adenosine.

Tumor-derived CD73 is a mechanism of tumor immune escape and tumor metastasis, and targeted therapy against CD73 can trigger adaptive anti-tumor immunity and inhibit metastasis of breast cancer.

References

- Zimmermann H. 5'-Nucleotidase: molecular structure and functional aspects. *Biochem J.* 1992 Jul 15;285 (Pt 2):345-65
- Koszalka P, Ozüyan B, Huo Y, Zerneck A, Flögel U, Braun N, Buchheiser A, Decking UK, Smith ML, Sévigny J, Gear A, Weber AA, Molojavyi A, Ding Z, Weber C, Ley K, Zimmermann H, Gödecke A, Schrader J. Targeted disruption of cd73/ecto-5'-nucleotidase alters thromboregulation and augments vascular inflammatory response. *Circ Res.* 2004 Oct 15;95(8):814-21
- Zhou P, Zhi X, Zhou T, Chen S, Li X, Wang L, Yin L, Shao Z, Ou Z. Overexpression of Ecto-5'-nucleotidase (CD73) promotes T-47D human breast cancer cells invasion and adhesion to extracellular matrix. *Cancer Biol Ther.* 2007 Mar;6(3):426-31
- Wang L, Zhou X, Zhou T, Ma D, Chen S, Zhi X, Yin L, Shao Z, Ou Z, Zhou P. Ecto-5'-nucleotidase promotes invasion, migration and adhesion of human breast cancer cells. *J Cancer Res Clin Oncol.* 2008 Mar;134(3):365-72
- Grünwald JK, Ridley AJ. CD73 represses pro-inflammatory responses in human endothelial cells. *J Inflamm (Lond).* 2010 Feb 5;7(1):10
- Zhi X, Wang Y, Zhou X, Yu J, Jian R, Tang S, Yin L, Zhou P. RNAi-mediated CD73 suppression induces apoptosis and cell-cycle arrest in human breast cancer cells. *Cancer Sci.* 2010 Dec;101(12):2561-9
- Serra S, Horenstein AL, Vaisitti T, Brusa D, Rossi D, Laurenti L, D'Arema G, Coscia M, Tripodo C, Inghirami G, Robson SC,

Gaidano G, Malavasi F, Deaglio S. CD73-generated extracellular adenosine in chronic lymphocytic leukemia creates local conditions counteracting drug-induced cell death. *Blood*. 2011 Dec 1;118(23):6141-52

Cappellari AR, Vasques GJ, Bavaresco L, Braganhol E, Battastini AM. Involvement of ecto-5'-nucleotidase/CD73 in U138MG glioma cell adhesion. *Mol Cell Biochem*. 2012 Jan;359(1-2):315-22

Wang H, Lee S, Nigro CL, Lattanzio L, Merlano M, Monteverde M, Matin R, Purdie K, Mladkova N, Bergamaschi D, Harwood C, Syed N, Szlosarek P, Briasoulis E, McHugh A, Thompson A, Evans A, Leigh I, Fleming C, Inman GJ, Hatzimichael E,

Proby C, Crook T. NT5E (CD73) is epigenetically regulated in malignant melanoma and associated with metastatic site specificity. *Br J Cancer*. 2012 Apr 10;106(8):1446-52

Wu XR, He XS, Chen YF, Yuan RX, Zeng Y, Lian L, Zou YF, Lan N, Wu XJ, Lan P. High expression of CD73 as a poor prognostic biomarker in human colorectal cancer. *J Surg Oncol*. 2012 Aug 1;106(2):130-7

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